Serial No. 08/955,572

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Kwon, Byoung	Examiner: C. Kaufman	
Serial No.:	08/948,764	Group Art Unit: 1646	
Filed:	October 10, 1997	Docket: 740.012US2	
Title:	NEW RECEPTOR AND RELATED PRODUCTS AND METHODS		

SUPPLEMENTAL DECLARATION UNDER 37 C.F.R. § 1.131(b)

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

I, Byoung Kwon declare and say as follows:

1. I am the named inventor of the subject matter claimed in the above-identified patent application, U.S. application Serial No. 08/948,764, filed on October 10, 1997.

2. I received a Certificate in 1968, a D.D.S. in 1972, and a M.S. in Microbiology in 1974, from Seoul National University, Seoul, Korea. In 1981, I received a Ph.D. in microbiology from the Medical College of Georgia, Augusta, Georgia. From 1981-1984, I was a postdoctoral fellow in the Department of Human Genetics at Yale University School of Medicine, New Haven, Connecticut. I was the Head of Medical Genetics at the Gutherie Research Institute, Sayre, Pennsylvania, from 1984-1988. From 1988-1993, I was an Associate Professor in the Department of Microbiology and Immunology, Indiana University School of Medicine, Indianapolis, Indiana. From 1993-1999, I was a Professor in that same Department. I am currently a Professor at Louisiana State University. I have authored or co-authored over 100 papers, primarily in the areas of the molecular basis for pigmentation and the identification and characterization of molecules involved in lymphocyte activation and proliferation.

3. I have reviewed the Goodwin et al. patent (U.S. Patent No. 5,674,704) and Schwarz et al. (Genbank Accession No: L12964) cited by the Examiner in the final Office Action dated January 12, 1999, and the Advisory Action dated July 30, 1999 and make this Declaration in support of the patentability of the claims of U.S. patent application Serial No. 08/948,764.

4. Prior to the April 22, 1993 publication date of Schwarz et al. and the May 7, 1993 filing date of the parent application to the Goodwin et al. patent, I had isolated and purified a portion of a human 4-1BB (H4-1BB) gene and thereafter proceeded diligently to characterize the full length gene. Also prior to the effective date of Schwarz et al. and the effective date of the Goodwin et al. patent, I had prepared DNA encoding a fusion protein comprising the extracellular domain of H4-1BB.

5. Schwarz et al. disclose the nucleotide sequence and inferred amino acid sequence of a human cDNA termed ILA. The nucleotide sequence of ILA encodes a polypeptide that has a single amino acid substitution relative to SEQ ID NO:2 of the present application.

6. The Goodwin et al. patent discloses an amino acid sequence of a H4-1BB polypeptide which is identical to the H4-1BB amino acid sequence disclosed in the above-identified application. Example 3 of the Goodwin et al. patent describes the preparation of DNA encoding a fusion protein that includes the 186 amino acids of H4-1BB including the signal sequence fused to Fc.

7. Exhibit A, attached hereto and incorporated by reference herein, is submitted as factual evidence of the reduction to practice of the invention in the United States prior to the effective date of the above-mentioned references.

8. As factual evidence that the invention was reduced to practice in the United States prior to the effective dates of Schwarz et al. and Goodwin et al., Exhibit A is a photocopy of certain pages from a laboratory notebook. The 5' portion of the H4-1BB cDNA, including sequences encoding the signal peptide and the entire extracellular domain, was amplified by a polymerase chain reaction (PCR) with two primers termed 5' and 3'. The 5' primer included a BglII site at the 5' end of the primer, and the 3' primer included a HindIII site at the 5' end of the 3' primer, to facilitate directional and positional cloning into a mammalian expression vector, APtag-1, that had been digested with BglII and HindIII. The sequence of the 5' primer was: 5' ATAGATCTATGGGAAACAGCTGTTAC 3', and the sequence of the 3' primer was: 5'

ATAAGCTTCGGAGAGTGTCCTGGCTC 3'. The introduction of the BglII-HindIII digested H4-1BB fragment into BglII-HindIII digested APtag-1 results in the introduction of the coding sequence of H4-1BB upstream of the coding sequence for human placental alkaline phosphatase (AP). Sheet 1 of Exhibit A indicates the reaction conditions employed to digest the amplified H4-1BB product with BglII and HindIII and to digest APtag-1 with those same enzymes. A portion of the products from these reactions were subjected to agarose gel electrophoresis. Sheet 2 of Exhibit A shows a photograph of that gel. The lane closest to the top of the sheet has the product(s) from the digestion of APtag-1 with HindIII and BglII while the lane beneath that lane has the product(s) from the digestion of the amplified H4-1BB product with HindIII and BglII. To prepare an expression vector comprising DNA encoding a fusion protein comprising an N-terminal portion of H4-1BB and AP, the products shown on the gel were ligated. The ligation reaction mixture is described on sheet 3 of Exhibit A. The experiments which produced Exhibit A were performed in my laboratory at Indiana University, Indianapolis, Indiana, USA. The material in Exhibit A which has been deemed to be irrelevant to evidence supporting the conception of the invention claimed in the above-identified application has been masked out on Exhibit A. Exhibit A is dated prior to April 22, 1993 (date masked out).

9. In order to prepare a fusion protein in which a portion of H4-1BB was linked in frame to AP, it is logical to conclude that the nucleotide sequence of H4-1BB was known. In particular, the amplification of a portion of the nucleic acid sequence of H4-1BB with primers, the selection of restriction enzymes that do not cleave DNA in the portion of the nucleic acid sequence of H4-1BB to be inserted into an expression vector, and the introduction of the digested DNA so that the coding sequence is linked in frame with the coding sequence of another protein, shows that the nucleotide sequence of H4-1BB was available. Thus, Exhibit A demonstrates that the invention claimed in the present application was reduced to practice prior to the effective date of Schwarz et al., i.e., April 22, 1993, and Goodwin et al., i.e., May 7, 1993.

10. I further declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made

are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: 1/3/2008

By: _____
Byoung Kwon

Consecutive digestion of AP-tag/BglII & HindIII

BglII digestion	19 ul
water	17 ul
React I	2 ul
HindIII	2 ul
	40 ul at 37°C

(purify by elutip method) 05:00

digestion of 4-1BB PCR products

4-1BB (5', 3')	16 ul
React 3	2 ul
spermidine	1 ul
BglII	1 ul
	20 ul

at 37°C 05:00

React 4	2 ul
water	16 ul
HindIII	2 ul
	40 ul

BEST AVAILABLE COPY

EXHIBIT
A
SHEET 2

Ligation

	exp.	self
APtag/HindIII..BglII (150ng/μl)	1 μl	1 μl
4-1BB(PCR)/HindIII-BglII (8ng/μl)	2 μl	—
5X buffer	2 μl	2 μl
water	4.5	6.5
ligase	0.5	0.5 μl
	10 μl	10.0 μl

F)

EXHIBIT
1 A
SHEETS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No.:	**740.013US3 (IU-0030)**
Inventors:	**Kwon, Byoung S.**
Serial No.:	**10/027,199**
Filing Date:	**December 20, 2001**
Examiner:	**Landsman, Robert S.**
Customer No.:	**26259**
Group Art Unit:	**1647**
Confirmation No.:	**2369**
Title:	**Receptor and Related Products and Methods**

"Express Mail" Label No. **EV593364199US**
Date of Deposit **December 23, 2004**
I hereby certify that this paper is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Mail Stop Fee Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

By _____
Typed Name: **Jane Massey Licata, Reg. No. 32,257**

Mail Stop Fee Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

AFFIDAVIT

In accordance with the conditions set forth by the Budapest Treaty the undersigned attorney of record hereby states, and affirms that:

(a) The *Escherichia coli* Human 4-1BBcDNA(pH4-1BB) related to the above referenced application has been deposited with, and accepted by an International Depository Authority under the provisions of the Budapest Treaty. The deposit was made on August 25, 1993 to the Agricultural Research Culture Collection (NRRL), International

Depositary Authority, 1815 N. University Street, Peoria, IL 61604. The Accession Number given by the International Depositary Authority is NRRL B-21131. All restrictions upon public access to this cell line will be irrevocably removed upon grant of a patent on this above referenced application. The Deposit will be maintained in a public depository for a period of thirty years after the date of deposit or five years after the last request for a sample or for the enforceable life of the patent, whichever is longer. The above-referenced cell line was viable at the time of the deposit. The Deposit will be replaced if viable samples cannot be dispensed by the depository.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted,

Jane Massey Licata
Registration No. 32,257

Date: **December 23, 2004**

Licata & Tyrrell P.C.
66 E. Main Street
Marlton, New Jersey 08053

(856) 810-1515

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSE OF PATENT PROCEDURE

INTERNATIONAL FORM

TO Dr. Bjong Kwon
Dept. of Microbiology & Immunology
Indiana University School of Medicine
635 Barnhill Drive, Room 255
Indianapolis, IN 46202-5120
NAME AND ADDRESS OF DEPOSITOR

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT
Issued pursuant to Rule 7.1 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page

I. IDENTIFICATION OF THE MICROORGANISM

Identification reference given by the DEPOSITOR:	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY:
Escherichia coli Human 4-1BBcDNA(pH4-1BB)	NRRL B-21131

II. SCIENTIFIC DESCRIPTION AND/OR PROPOSED TAXONOMIC DESIGNATION

The microorganism identified under I. above was accompanied by:

[ ] a scientific description

[X] a proposed taxonomic designation

(Mark with a cross where applicable)

III. RECEIPT AND ACCEPTANCE

This International Depositary Authority accepts the microorganism identified under I. above, which was received by it on August 25, 1993 (date of the original deposit)[1]

IV. RECEIPT OF REQUEST FOR CONVERSION

The microorganism identified under I. above was received by this International Depositary Authority on (date of the original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was received by it on (date of receipt of request for conversion)

V. INTERNATIONAL DEPOSITARY AUTHORITY

Name: Agricultural Research Culture Collection (NRRL) International Depositary Authority Address: 1815 N. University Street Peoria, Illinois 61604 U.S.A.	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s): Date: 9-30-93

[1] Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired.